

Atty Docket No.: R0130D-CON  
USSN: 10/823,012

### REMARKS

Claims 48 and 53-62 are pending in the above-identified patent application. Claims 48 and 50 are amended herein. Claims 53-52 are withdrawn from consideration.

#### 1. Double Patenting

Claims 48-52 and 54 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4, 8, 10, 12-14, 18, 20, 27-30, 44-47 56-58, 60 and 64 of US 5,952,362, and over claims 1-10, 17 and 26-39 of US 6,756,395. The Examiner noted that the instantly claimed compounds are generically described in the claims of US 6,756,395, and are positional isomers of compounds claimed in US 5,952,362.

The Applicants submit herewith a terminal disclaimer (37 CFR §1.321(c)) to disclaim any patent term which extends beyond that of US 6,756,395.

Applicants believe that the instantly claimed compound is non-obvious and patentable over US 5,952,362 for the reasons provided below.

#### 2. Rejection Under 35 USC §103

Claims 48-52 and 54 were rejected under 35 USC §103 as unpatentable over Courmoyer et al., US 5,952,362. The Examiner stated that US 5,952,362 discloses and claims structural isomers of the compounds claimed in the above-identified application. The Examiner noted in particular that US 5,952,362 discloses compounds having a phenyl ring with a sulfonamido group attached *meta* to the imidazolinylmethyl group, while the instantly claimed compounds include a phenyl ring with with a sulfonamide group attached *para* to the imidazolinylmethyl group. The Examiner stated that nothing unobvious is seen in substituting the known isomer of US 5,952,362 with the presently claimed isomer, since structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results.

The Examiner stated that Applicants' arguments filed on October 20 2005 were considered but were not found persuasive. The Examiner stated in particular that Applicants' showing of unexpected results was not persuasive because: (1) the showing

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and data were not presented in a declaration under 37 CFR §1.132; (2) the demonstrated activity of good uroselectivity could not be found in the specification; and (3) the showing was not commensurate in scope of the instant claimed invention, citing MPEP 716.02(d). The Examiner also indicated that US 5,952,362 has a common inventor and constitutes prior art only under 35 USC §102(e), and that the rejection may be overcome by declarations under 37 CFR §1.132, §1.131 or §1.130, or a showing of common ownership under 35 USC §103(c). Applicants address each of these points below.

a. Showing and data not presented in a declaration under 37 CFR §1.132

The Examiner stated that Applicants' showing of unexpected results was not persuasive because the showing and data were not presented in a declaration under 37 CFR §1.132.

Applicants submit herewith a Declaration under 37 CFR §1.132 signed by co-inventor Counde O-Yang showing Applicants' unexpected result.

b. Demonstrated activity of good uroselectivity not found in specification

The Examiner further stated that Applicants' showing of unexpected results was not persuasive because the demonstrated activity of good uroselectivity could not be found in the specification.

The Applicants respectfully disagree with the Examiner. Uroselectivity, or selective control of urethral activity relative to unwanted blood pressure effects, is described in Applicants' specification. At page 32, paragraph number 116, it is noted that Applicants alpha 1A adrenoceptor agonist compounds were "evaluated *in vivo* in anesthetized female rabbits to assess urethral activity relative to diastolic blood pressure effects" (i.e., to assess uroselectivity). Experimental Example number 8 (page 58 paragraph numbers 201-205) describes an experimental protocol for measuring intraurethral pressure (IUP) and mean arterial pressure (MAP) for determining uroselectivity. At page 2, paragraph number seven, Applicants note the lack of selectivity of prior art alpha 1 adrenoceptor modulators results in undesired side effects such as increase in blood pressure.

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Applicants note that uroselectivity is well recognized by those skilled in the art as a desirable property for alpha 1A adrenoceptor modulators. For example, Ruffolo et al., in "Adrenoceptor Pharmacology: Urogenital Applications", *European Urology* Vol. 36(Suppl. 1) pp 17-22 (1999), state (in the Abstract) that

"Research efforts are ongoing to identify agents of this class [1 Adrenoceptor agonists] having a selective action on urethral versus vascular smooth muscle, in order to produce a greater effect on the urethra without producing dose-limiting increases in blood pressure."

Ruffolo et al. further note, in discussing urinary incontinence on page 20, that

"[t]he  $\alpha$ 1-adrenoceptor agonists currently used for stress incontinence do not differentiate between vascular and urethral  $\alpha$ 1-adrenoceptors, and therefore increases in blood pressure may be observed with these drugs. However, in vivo [12] and in vitro [44] data support the notion that it is possible to increase selectively urethral vis-a-vis vascular tone."

Applicants also respectfully believe that there is no requirement, in the MPEP or Title 37 Rules, that evidence of unexpected benefit or result must be included in the specification in order for such evidence to overcome a *prima facie* obviousness rejection. MPEP § 716.02(a)(II) provides that "Evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness." "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." No set number of examples of superiority is required. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Applicants believe that the unexpected superior uroselectivity described in the Rule 132 Declaration of Dr. Counde O-Yang makes Applicants claimed compounds patentably distinct from the compounds described in US 5,952,362.

c. Showing not commensurate in scope with the instant claimed invention

The Examiner indicated that Applicants showing of unexpected benefit was not commensurate in scope with Applicants' claims. Applicants note that independent claim is quite narrow in scope and includes only two variables, R<sup>1</sup> and R<sup>4</sup>, R<sup>1</sup> limited to alkyl,

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and R<sup>4</sup> limited to hydrogen, halo, alkyl, alkoxy, and hydroxy. Applicants have amended claim 48 to delete the recitation of "cycloalkylalkyloxy" with respect to the variable R<sup>4</sup>. No set number of examples of superiority is required, as noted above. In view of the narrow scope of Applicants claims, Applicants respectfully believe that the showing of unexpected benefit by the Rule 132 Declaration submitted herewith is commensurate in scope with the claims.

d. US 5,952,362 as prior art only under 35 USC §102(e)

The Examiner indicated that US 5,952,362 has a common inventor and constitutes prior art only under 35 USC §102(e), and that the rejection may be overcome by declarations under 37 CFR §1.132, §1.131 or §1.130, or a showing of common ownership under 35 USC §103(c).

The Applicants note that US 5,952,362 was granted on September 14 1999. The instant application has an earliest priority date of April 23 2002 based on US Provisional Application No. 60/374,700. Since US 5,952,362 was granted more than one year before Applicants' earliest priority date, Applicants believe that US 5,952,362 is prior art under 35 USC §102(b). Otherwise Applicants would seek to disqualify US 5,952,362 as prior art under 35 USC §103(c) as recommended by the Examiner.

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### CONCLUSION

In view of the foregoing, Applicants believe that the pending claims in the above identified patent application are patentable over the prior art of record and in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-354-7540.

Please charge the fees for Request for Continued Examination (37 C.F.R. §1.17(e)), fee for a three month Extension of time (37 C.F.R. §§ 1.17(a)(3)), and fee for terminal disclaimer ((37 CFR §1.20(d), to Deposit Account No. 18-1700.

Respectfully submitted,



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